

WHAT IS CLAIMED IS:

1. A humanized anti-VEGF antibody which binds human VEGF with a  $K_d$  value of no more than about  $1 \times 10^{-8}M$ .
2. A humanized anti-VEGF antibody which binds human VEGF with a  $K_d$  value of no more than about  $5 \times 10^{-9}M$ .
3. A humanized anti-VEGF antibody which has an ED50 value of no more than about 5nM for inhibiting VEGF-induced proliferation of endothelial cells *in vitro*.
4. A humanized anti-VEGF antibody which inhibits VEGF-induced angiogenesis *in vivo*.
5. The humanized anti-VEGF antibody of claim 4 wherein 5mg/kg of the antibody inhibits at least about 50% of tumor growth in an A673 *in vivo* tumor model.
6. The humanized anti-VEGF antibody of claim 1 having a heavy chain variable domain comprising the following hypervariable region amino acid sequences: CDRH1 (GYX<sub>1</sub>FTX<sub>2</sub>YGMN, wherein X<sub>1</sub> is T or D and X<sub>2</sub> is N or H; SEQ ID NO:128), CDRH2 (WINTYTGEPTYAADFQR; SEQ ID NO:2) and CDRH3 (YPX<sub>1</sub>YYGX<sub>2</sub>SHWYFDV, wherein X<sub>1</sub> is Y or H and X<sub>2</sub> is S or T; SEQ ID NO:129).
7. The humanized anti-VEGF antibody of claim 6 comprising the amino acid sequence of SEQ ID NO:7.
8. The humanized anti-VEGF antibody of claim 6 having a heavy chain variable domain comprising the following hypervariable region amino acid sequences: CDRH1 (GYTFTNYGMN; SEQ ID NO:1), CDRH2 (WINTYTGEPTYAADFQR; SEQ ID NO:2) and CDRH3 (YPHYYGSSHWYFDV; SEQ ID NO:3).

9. The humanized anti-VEGF antibody of claim 1 having a light chain variable domain comprising the following hypervariable region amino acid sequences: CDRL1 (SASQDISNYLN; SEQ ID NO:4), CDRL2 (FTSSLHS; SEQ ID NO:5) and CDRL3 (QQYSTVPWT; SEQ ID NO:6).

10. The humanized anti-VEGF antibody of claim 9 comprising the amino acid sequence of SEQ ID NO:8.

11. The humanized anti-VEGF antibody of claim 1 having a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:7 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:8.

12. An anti-VEGF antibody light chain variable domain comprising the amino acid sequence: DIQX<sub>1</sub>TQSPSSLSASVGDRVTITCSASQDISNYLNWYQQ KPGKAPKVLITYFTSSLHSGVPSRFS GSGSGTDFTLTISLQPEDFATYYCQQYSTVPWTFGQGGTKVEIKR (SEQ ID NO:124), wherein X<sub>1</sub> is M or L.

13. An anti-VEGF antibody heavy chain variable domain comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAASGYX<sub>1</sub>FTX<sub>2</sub>YGMNWVRQAPGKGLEWGWINTYTGEPT YAADFKRRFTFSLDTSKSTAYLQMNSLRAEDTAVYYCAKYPX<sub>3</sub>YYGX<sub>4</sub>SHWYFDVWGQGLTV TVSS (SEQ ID NO:125), wherein X<sub>1</sub> is T or D; X<sub>2</sub> is N or H; X<sub>3</sub> is Y or H and X<sub>4</sub> is S or T.

14. A variant of a parent anti-VEGF antibody, wherein said variant binds human VEGF and comprises an amino acid substitution in a hypervariable region of a heavy chain variable domain of said parent antibody.

15. The variant of claim 14 wherein said parent antibody is a human or humanized antibody.

16. The variant of claim 14 which binds human VEGF with a K<sub>d</sub> value of no more than about 1 x 10<sup>-8</sup>M.

17. The variant of claim 14 which binds human VEGF with a  $K_d$  value of no more than about  $5 \times 10^{-9}M$ .
18. The variant of claim 14 wherein the substitution is in CDRH1 of the heavy chain variable domain.
19. The variant of claim 14 wherein the substitution is in CDRH3 of the heavy chain variable domain.
20. The variant of claim 14 which has amino acid substitutions in both CDRH1 and CDRH3.
21. The variant of claim 14 which binds human VEGF with a  $K_d$  value less than that of said parent antibody.
22. The variant of claim 14 which has an ED50 value for inhibiting VEGF-induced proliferation of endothelial cells *in vitro* which is at least about 10 fold lower than that of said parent antibody.
23. The variant of claim 18 wherein the CDRH1 comprises the amino acid sequence: GYDFTHYGMN (SEQ ID NO:126)
24. The variant of claim 19 wherein the CDRH3 comprises the amino acid sequence: YPYYGTSHWYFDV (SEQ ID NO:127).
25. The variant of claim 14 wherein the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO:116.
26. The variant of claim 25 further comprising the light chain variable domain amino acid sequence of SEQ ID NO:124.

27. The variant of claim 26 comprising the light chain variable domain amino acid sequence of SEQ ID NO:115.

28. The humanized anti-VEGF antibody of claim 1 which is a full length antibody.

29. The humanized anti-VEGF antibody of claim 28 which is a human IgG.

30. The humanized anti-VEGF antibody of claim 1 which is an antibody fragment.

31. The antibody fragment of claim 30 which is a Fab.

32. A composition comprising the humanized anti-VEGF antibody of claim 1 and a pharmaceutically acceptable carrier.

33. A composition comprising the variant anti-VEGF antibody of claim 14 and a pharmaceutically acceptable carrier.

34. Isolated nucleic acid encoding the antibody of claim 1.

35. A vector comprising the nucleic acid of claim 34.

36. A host cell comprising the vector of claim 35.

37. A process of producing a humanized anti-VEGF antibody comprising culturing the host cell of claim 36 so that the nucleic acid is expressed.

38. The process of claim 37 further comprising recovering the humanized anti-VEGF antibody from the host cell culture.

